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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/890,323	12/10/2001	Douglas P. Cerretti	2517-USA	9524

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/890,323	CERRETTI, DOUGLAS P.
Examiner	**Art Unit**
William W. Moore	1652

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,13 and 45-68* is/are pending in the application.

4a) Of the above claim(s) *45,47,51 and 60-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,13,46,48-50 and 52-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *4-6,13 and 45-68* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

DETAILED ACTION

Response to Amendment

Applicant's Amendment B, Paper No. 14 filed December 23, 2002, has been entered, replacing the original title with an amended title, canceling the non-elected claims 1-3, 7-12 and 14-44, amending claims 4 and13, and adding new claims 45-68. The amended claims 4 and 13 and the newly submitted claims 45-68 are directed, wholly or in part, to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicant elected Group XXII for prosecution in Paper No. 9 filed April 4, 2002, with traverse and Applicant's traversal on the grounds that the integral SVPH-1a, SVPH-1b and SVPH-1c polypeptides share a common, special technical feature, e.g., complete identity throughout a common amino acid sequence of 750 amino acids was persuasive, permitting rescission of the restriction requirement between Groups XXII-XXIV. Applicant's further arguments in traversal of the restriction requirement mailed March 15, 2002, as between Groups XXII and any of Groups XXV-XXXIV were not persuasive and the restriction requirement removing subject matters of these further Groups from consideration was made FINAL. Yet clause (b) of the amended claim 4, the terminal phrase of the amended claim 13, each of the new claims 45, 47, 51, clause (b) of claim 53, and claims 60-68 describe subject matters that are included in the non-elected and non-examined heterochimeric or oligomeric subject matters of Groups XXIX-XXXI set forth in the restriction requirement of March 15, 2002. Since applicant has received an action on the merits for the originally presented invention, that invention has been constructively elected by original presentation for prosecution on the merits. Claims 45, 47, 51, and 60-68 are accordingly withdrawn from consideration as being directed to a non-elected invention and claims 4-6, 13, 46, 48-50, and 52-59 are examined herein

thereof, encoded by nucleic acid sequences specified in clauses (a), (c) and (d) of claims 4 and 53. See 37 CFR 1.142(b) and MPEP § 821.03. Cancellation of claims 45, 47, 51, and 60-68, and the deletion of clauses (b) of claims 4 and 53 as well as the deletion of the terminal phrase of claim 13, corresponding to non-elected subject matter, is required in response to this final communication.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 4-6, 13, 46, 48-50 and 52-59 are for reasons of record rejected under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

Applicant's arguments filed December 23, 2002, have been fully considered but they are not persuasive. Applicant suggests at page 6 of Paper No. 14 that claim limitations requiring disintegrin activity added by amendments of Paper No. 14, combined with the presence of disintegrin domains in amino acid sequences of elected and examined integral SVPH-1 polypeptides, or variants thereof, and the corresponding presence of a disintegrin domain in polypeptide products described in claims 18-34 of U.S. Patent 6,485,956, made of record herewith, is a sufficient basis for inferring utility for an elected, integral, SVPH-1 polypeptide, or variant thereof. The specification does not disclose, however, that the disintegrin domain common to the three SVPH-1 polypeptides disclosed herein binds any integrin, or has some other specific biological activity, or that integral SVPH-1a, SVPH-1b, and SVPH-1c polypeptides claimed herein have any specific biological activity. The issued patent discloses a native SVPH-8 polypeptide sharing but 47% overall sequence identity with, e.g., the SVPH-1a amino acid sequence herein and the SVPH-8 polypeptide disintegrin domain has just 67% amino acid sequence identity with the common disintegrin domain of the three SVPH-1 polypeptides disclosed herein. Applicant does not argue, and

polypeptide during prosecution of the application issuing as the '956 patent is specifically shared by any of the SVPH-1a, SVPH-1b, or SVPH-1c polypeptides disclosed herein, or by their common disintegrin domain.

A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. The slight degree of similarity between the integral SVPH-8 polypeptide and the integral SVPH-1a, SVPH-1b, or SVPH-1c polypeptides and the limited degree of similarity between the SVPH-8 polypeptide disintegrin domain and the disintegrin domain common to the SVPH-1a, SVPH-1b, or SVPH-1c polypeptides cannot establish a specific *in vitro* utility for an integral SVPH-1a, SVPH-1b, or SVPH-1c polypeptide. A method of using a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification is silent about the nature of a specific cellular process that might require the presence or activity of any of the three SVPH-1 polypeptides disclosed herein and fails to indicate the specific nature of a common disintegrin-like activity of any of these related products, within a cell or acts outside a cell, that might make the argued utility substantial. Thus the rejection of record is sustained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6, 13, 46, 48-50 and 52-59 are also rejected for reasons of record under 35 U.S.C. §112, first paragraph. Applicant's arguments filed December 23, 2002, have been fully considered but they are not persuasive. Specifically, one skilled in the art clearly

specific

Claims 4-6, 46, 48-50 and 52-59 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This new ground of rejection is necessitated by Applicant's amendments of Paper No. 14. The specification fails to exemplify or describe the preparation of the subject matters of divergent SVPH-1 products indicated by clause (c) of claims 4 and 53, which subject matters are incorporated in claims 5, 6, 46, 52 and 54-59 through dependency from claims 4 and 53. Because a nucleotide sequence capable of hybridizing to one of SEQ IDs NOs:7, 8 or 9 with the conditions recited in clause (c) may vary by relative nucleotide sequence insertions, deletions, and substitutions at as much as 33% of the positions in the nucleic acid sequences of SEQ IDs NOs:7, 8 or 9, the rejected claims reach generic proteins that differ at over 33% of the amino acid positions of the disclosed amino acid sequences of SEQ IDs NOs:12, 13 and 14 where the nucleotide sequence alterations are only substitutions and occur in the first and second codon positions. Yet neither the claims nor the specification describe where amino acid sequence differences may occur save for the terminal sixteen amino acids of SEQ ID NO:12 where SEQ IDs NOs:13 and 14 vary by amino acid sequence deletions/and or substitutions - a scant 2% of the amino acid sequence of the longer SEQ ID NO:12 - nor what the differences might be among the remaining 98% of the amino acid sequence common to SEQ IDs NOs:12, 13 and 14. The specification does not otherwise disclose or suggest the nature or source of any of the generic proteins that meet the limitations of the claims. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification fails to furnish any relevant identifying characteristics for the

sequences of SEQ IDs NOs:12, 13 and 14, nor does it provide any characteristic that permits a correlation between the undisclosed structures of any proteins within the nearly astronomical genus that meet structural limitations of the claims and the disclosed amino acid sequences of SEQ IDs NOs:12, 13 and 14.

In addressing the issue of whether disclosure of the structure of a polypeptide of one animal species could adequately describe the molecular structure of functionally similar polypeptides of other animal species, the Court of Appeals for the Federal Circuit held that the specification must describe a claimed invention with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Indeed, the claims rejected herein are, like the claims invalidated by the appellate panel in *University of California v. Eli Lilly*, designed to embrace other, as yet unknown, polypeptides of undisclosed mammals or other vertebrates. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of any of an undisclosed generic protein to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the generic polypeptides of claims 4-6, 46, 48-50 and 52-59.

Claims 4-6, 13, 46, 48-50 and 52-59 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while enabling for an SVPH-1 polypeptide that differs from the amino acid sequences of SEQ IDs NOs:12, 13 and 14 by amino acid sequence deletions and substitutions in the carboxyl-terminal sixteen amino acids of SEQ ID NO:12,

acid substitutions, deletions and insertions, or combinations thereof at as many as 33% of the amino acid positions of any of SEQ IDs NOs: 12, 13 and 14 in any region thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

This new ground of rejection is necessitated by Applicant's amendments of Paper No. 14. Claims 4-6, 13, 46, 48-50 and 52-59 contemplate an arbitrary assignment of any or all of amino acid substitutions, additions or deletions in a polypeptide at as many as 33% of the amino acid positions disclosed in the amino acid sequences of SEQ IDs NOs: 12, 13 and 14. This rejection is stated under the first paragraph of the statute because the specification cannot support introduction of as many as 252 amino acid substitutions, additions and/or deletions in the amino acid sequences of SEQ IDs NOs: 12, 13 and 14. Indeed, neither the prior art made of record herewith nor Applicant's specification can identify, taken together, hundreds of amino acid positions in the amino acid sequences of vertebrate human metalloprotease-disintegrins that might be altered, nor teach the nature of alterations that may be made, which permit a resulting polypeptide to retain its native biological function(s). Mere sequence perturbation cannot enable the design and preparation of nucleotide sequences encoding a myriad of divergent enzymes and provide the public with a nucleotide sequence encoding an enzyme that retains its native function. This is well demonstrated by the publication of Seffernick et al., 2001, **Journal of Biochemistry**, Vol. 183, pages 2405-2410, made of record herewith, who teach that the alteration of 9 amino acids in a sequence of 475 amino acids, a scant 2% of the native amino acid positions, in a deaminase will suffice to alter its substrate specificity and require it to catalyze different reactions even though, p. 2409, these alterations do not at all alter its tertiary structure and are spread throughout its primary structure.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed

claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).

The Federal Circuit has also considered whether definitional statements might enable a claim scope argued to extend beyond a disclosed gene product having its native amino acid sequence to embrace a specific variant gene product encoded by a specifically-altered DNA sequence. *Genentech, Inc. v. The Wellcome Found. Ltd.*, 29 F.3d 1555, 31 USPQ2d 1161 (Fed. Cir. 1994). The court held that only a narrow structural and functional definition was enabling precisely because the sweeping definitions of scope in the patent specification could not reasonably have been relied upon by the PTO in issuing the patent. *Genentech*, 29 F.3d 15 at 1564-65, 31 USPQ2d at 1168. Applying the "*Forman*" factors discussed in *Wands*, ***supra***, to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequences of proteases of SEQ IDs NOs: 12, 13 and 14 to any extent, let alone the extent recited in the claims that would also permit retention of a function

b) the specification lacks working examples wherein proteases of any of SEQ IDs NOs: 12, 13 and 14, are altered to any extent, let alone the extent indicated in the amended claims, that would also permit retention of a function required by the claims herein as amended in Paper No. 14,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support alterations that would also permit retention of a function required by the claims herein as amended in Paper No. 14, and,

d) unpredictability exists in the art where no members of the class of vertebrate metalloprotease-disintegrins represented by amino acid sequences of SEQ IDs NOs: 12, 13 and 14, have had even a few amino acids specifically identified for concurrent modification yet permitting retention of a function required by the claims herein as amended in Paper No. 14.

Thus the scope of the subject matter embraced by clauses (c) of claims 4 and 53 - and by claims 5, 6, 46, 52 and 54-59 in view of dependency therefrom - is unsupported by the present specification even if taken in combination with teachings available in the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct FAX telephone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
March 17, 2003